

What is claimed is:

1. A method of treating or preventing nerve cell death or degeneration comprising administering to a mammal suffering from or susceptible to nerve cell death or degeneration a therapeutically effective amount of GDF-1 or a fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof.

2. A method of claim 1 wherein the nerve cell death or degeneration is caused by brain or spinal cord trauma, brain or spinal cord ischemia, retinal ischemia, hypoxia or hypoglycemia.

3. A method of claim 1 or 2 wherein GDF-1 or a fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof is administered after the mammal has suffered nerve cell death or degeneration.

4. A method of claim 1 or 2 wherein GDF-1 or a fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof is administered to the mammal for at least about two weeks after the mammal has suffered nerve cell death or degeneration.

5. A method of treating a mammal suffering from or susceptible to stroke or heart attack comprising administering to the mammal a therapeutically effective amount of GDF-1 or a fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof.

6. A method of claim 5 wherein GDF-1 or fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof is administered after the mammal has suffered stroke or heart attack.

7. A method of claim 5 wherein GDF-1 or fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof is administered to the mammal for at least about two weeks after the mammal has suffered stroke or heart attack.

8. A method of treating a mammal suffering from or susceptible to brain or spinal cord trauma or ischemia comprising administering to the mammal a therapeutically effective amount of GDF-1 or a fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof.

9. A method of claim 8 wherein GDF-1 or fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof is administered after the mammal has suffered brain or spinal cord trauma or ischemia.

10. A method of claim 8 wherein GDF-1 or fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof is administered to the mammal for at least about two weeks after the mammal has suffered brain or spinal cord trauma or ischemia.

11. A method of treating a mammal suffering from or susceptible to decreased blood flow or nutrient supply to retinal tissue or optic nerve, or retinal ischemia or trauma, or optic nerve injury, or glaucoma, comprising administering to the mammal a therapeutically effective amount of GDF-1 or a fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof.

12. A method of claim 11 wherein GDF-1 or fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof is administered after the mammal has suffered decreased blood flow or nutrient supply to retinal tissue or optic nerve, or retinal ischemia or trauma, or optic nerve injury, or glaucoma.

13. A method of claim 11 wherein GDF-1 or fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof is administered to the mammal for at least about two weeks after the mammal has suffered decreased blood flow or nutrient supply to retinal tissue or optic nerve, or retinal ischemia or trauma, or optic nerve injury, or glaucoma.

14. A method of treating a mammal suffering from or susceptible to post-surgical neurological deficits or neurological deficits associated with cardiac arrest, comprising administering to the mammal a therapeutically effective amount of GDF-1 or a fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof.

15. A method of claim 14 wherein GDF-1 or fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof is administered after the mammal has suffered a post-surgical neurological deficit or neurological deficit associated with cardiac arrest.

16. A method of claim 14 wherein GDF-1 or fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof is administered to the mammal for at least about two weeks after the mammal has suffered a post-surgical neurological deficit or neurological deficit associated with cardiac arrest.

17. A method of treating a mammal suffering from or susceptible to peripheral nerve damage, comprising administering to the mammal a therapeutically effective amount of GDF-1 or a fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof.

18. A method of claim 17 wherein GDF-1 or fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof is administered after the mammal has suffered peripheral nerve damage.

19. A method of claim 17 wherein GDF-1 or fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof is administered to the mammal for at least about two weeks after the mammal has suffered peripheral nerve damage.

20. A method of treating a neurodegenerative disease or a neuropathy comprising administering to a mammal suffering from or susceptible to said disease a therapeutically effective amount of GDF-1 or a fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof.

21. A method of treating Alzheimer's disease, Parkinson's disease, Huntington's Disease, Amyotrophic Lateral Sclerosis, Down's Syndrome, Korsakoff's disease, or epilepsy, comprising administering to a mammal suffering from or susceptible to said disease a therapeutically effective amount of GDF-1 or a fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof.

22. A method of improving functional capability of a mammal that has suffered nerve cell death or degeneration, comprising administering to the mammal a therapeutically effective amount of GDF-1 or a fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof.

23. A method of claim 22 wherein GDF-1 or fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof is administered to the mammal for at least about two weeks after the mammal has suffered the nerve cell death or degeneration.

24. A method of improving functional capability of a mammal that has suffered a neurodegenerative disease or a neuropathy, comprising administering to the mammal a therapeutically effective amount of GDF-1 or a fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof.

25. A method of claim 24 wherein the mammal is suffering from Alzheimer's disease, Parkinson's disease, Huntington's disease, Amyotrophic Lateral Sclerosis, down's Syndrome, Korsakoff's disease, or epilepsy.

26. A method of any one of claims 1-25 wherein GDF-1 or a fragment or derivative thereof is administered to the mammal.

27. A method of claim 26 wherein the administered GDF-1 is encoded by SEQ ID NO:1.

28. A method of claim 26 wherein the administered GDF-1 or fragment or derivative thereof is encoded by a nucleic acid that comprises a sequence that has at least about 70% sequence identity to SEQ ID NO:1.

29. A method of claim 26 wherein the administered GDF-1 or fragment or derivative thereof is encoded by a nucleic acid that comprises a sequence that has at least about 80%, 90% or 95% sequence identity to SEQ ID NO:1.

30. A method of claim 26 wherein the administered GDF-1 or fragment or derivative thereof is encoded by a sequence that hybridizes to SEQ ID NO:1 under normal stringency conditions.

31. A method of claim 26 wherein the administered GDF-1 or fragment or derivative thereof is encoded by a sequence that hybridizes to SEQ ID NO:1 under high stringency conditions.

32. A method of claim 26 wherein the administered GDF-1 or fragment or derivative has at least about 70% sequence identity to SEQ ID NO:2.

33. A method of claim 26 wherein the administered GDF-1 or fragment or derivative has at least about 80%, 90% or 95% sequence identity to SEQ ID NO:2.

34. A method of claim 26 wherein the administered GDF-1 has the sequence shown in SEQ ID NO:2.

35. A method of any one of claims 1-25 wherein a nucleic acid encoding GDF-1 or a fragment or derivative thereof is administered to the mammal.

36. A method of claim 35 wherein the nucleic acid is SEQ ID NO:1, or the complement thereof.

37. A method of claim 35 wherein the nucleic acid has at least about 70 percent homology to SEQ ID NO:1, or the complement thereof.

38. A method of claim 35 wherein the nucleic acid has at least about 80%, 90% or 95% homology to SEQ ID NO:1, or the complement thereof.

39. A method of claim 35 wherein the nucleic acid comprises a sequence that hybridizes to SEQ ID NO:1 under normal stringency conditions.

40. A method of claim 35 wherein the nucleic acid comprises a sequence that hybridizes to SEQ ID NO:1 under high stringency conditions.

41. A method of any one of claims 1-40 wherein the administered GDF-1 fragment or derivative, or the administered nucleic acid encodes a GDF-1 fragment or derivative exhibits at least about a 10% reduction in infarct volume in an *in vivo* cerebral ischemia assay.

42. A method of treating or preventing nerve cell death or degeneration comprising administering to a mammal suffering from or susceptible to nerve cell death or degeneration a therapeutically effective amount of 1) GDF-1 or fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof, and 2) neurotrophin-3 or nucleic acid encoding neurotrophin-3.

43. A method of claim 42 wherein the nerve cell death or degeneration is caused by brain or spinal cord trauma, brain or spinal cord ischemia, retinal ischemia, hypoxia or hypoglycemia.

44. A method of claim 42 or 43 wherein the effective amount of 1) and 2) is administered after the mammal has suffered nerve cell death or degeneration.

45. A method of claim 42 or 43 wherein the effective amount of 1) and 2) is administered to the mammal for at least about two weeks after the mammal has suffered nerve cell death or degeneration.

46. A method of treating a mammal suffering from or susceptible to stroke or heart attack comprising administering to the mammal a therapeutically effective amount of 1) GDF-1 or fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a

fragment or derivative thereof, and 2) neurotrophin-3 or nucleic acid encoding neurotrophin-3.

47. A method of claim 46 wherein the effective amount of 1) and 2) is administered after the mammal has suffered stroke or heart attack.

48. A method of claim 46 wherein the effective amount of 1) and 2) is administered to the mammal for at least about two weeks after the mammal has suffered stroke or heart attack.

49. A method of treating a mammal suffering from or susceptible to brain or spinal cord trauma or ischemia comprising administering to the mammal a therapeutically effective amount of 1) GDF-1 or a fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof, and 2) neurotrophin-3 or nucleic acid encoding neurotrophin-3.

50. A method of claim 49 wherein the effective amount of 1) and 2) is administered after the mammal has suffered brain or spinal cord trauma or ischemia.

51. A method of claim 49 wherein the effective amount of 1) and 2) is administered to the mammal for at least about two weeks after the mammal has suffered brain or spinal cord trauma or ischemia.

52. A method of treating a mammal suffering from or susceptible to decreased blood flow or nutrient supply to retinal tissue or optic nerve, or retinal ischemia or trauma, or optic nerve injury, or glaucoma, comprising administering to the mammal a therapeutically effective amount of 1) GDF-1 or fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof, and 2) neurotrophin-3 or nucleic acid encoding neurotrophin-3.



53. A method of claim 52 wherein the effective amount of 1) and 2) is administered after the mammal has suffered decreased blood flow or nutrient supply to retinal tissue or optic nerve, or retinal ischemia or trauma, or optic nerve injury, or glaucoma.

54. A method of claim 52 wherein the effective amount of 1) and 2) is administered to the mammal for at least about two weeks after the mammal has suffered decreased blood flow or nutrient supply to retinal tissue or optic nerve, or retinal ischemia or trauma, or optic nerve injury, or glaucoma.

55. A method of treating a mammal suffering from or susceptible to post-surgical neurological deficits or neurological deficits associated with cardiac arrest, comprising administering to the mammal a therapeutically effective amount of 1) GDF-1 or fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof, and 2) neurotrophin-3 or nucleic acid encoding neurotrophin-3.

56. A method of claim 55 wherein the effective amount of 1) and 2) is administered after the mammal has suffered a post-surgical neurological deficit or neurological deficit associated with cardiac arrest.

57. A method of claim 55 wherein the effective amount of 1) and 2) is administered to the mammal for at least about two weeks after the mammal has suffered a post-surgical neurological deficit or neurological deficit associated with cardiac arrest.

58. A method of treating a mammal suffering from or susceptible to peripheral nerve damage, comprising administering to the mammal a therapeutically effective amount of GDF-1 or fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof, and 2) neurotrophin-3 or nucleic acid encoding neurotrophin-3.

59. A method of claim 58 wherein the effective amount of 1) and 2) is administered after the mammal has suffered peripheral nerve damage.

60. A method of claim 58 wherein the effective amount of 1) and 2) is administered to the mammal for at least about two weeks after the mammal has suffered peripheral nerve damage.

61. A method of treating a neurodegenerative disease or a neuropathy comprising administering to a mammal suffering from or susceptible to said disease a therapeutically effective amount of 1) GDF-1 or a fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof, and 2) neurotrophin-3 or nucleic acid encoding neurotrophin-3.

62. A method of treating Alzheimer's disease, Parkinson's disease, Huntington's Disease, Amyotrophic Lateral Sclerosis, Down's Syndrome, Korsakoff's disease, or epilepsy, comprising administering to a mammal suffering from or susceptible to said disease a therapeutically effective amount of 1) GDF-1 or a fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof, and 2) neurotrophin-3 or nucleic acid encoding neurotrophin-3.

63. A method of improving functional capability of a mammal that has suffered nerve cell death or degeneration, comprising administering to the mammal a therapeutically effective amount of 1) GDF-1 or a fragment or derivative thereof, or a nucleic acid encoding GDF-1 or a fragment or derivative thereof, and 2) neurotrophin-3 or nucleic acid encoding neurotrophin-3.

64. A method of claim 63 wherein 1) and 2) are administered to the mammal for at least about two weeks after the mammal has suffered the nerve cell death or degeneration.

65. A method of claim 63 or 64 wherein the mammal has suffered brain or spinal cord trauma or ischemia, stroke, heart attack, hypoxia, hypoglycemia, retinal ischemia, or peripheral nerve damage.

66. A method of improving functional capability of a mammal that is suffering from a neurodegenerative disease or a neuropathy, comprising administering to the mammal a therapeutically effective amount of 1) GDF-1 or a fragment or derivative thereof, and 2) neurotrophin-3 or nucleic acid encoding neurotrophin-3.

67. The method of claim 66 wherein the mammal is suffering from Alzheimer's disease, Parkinson's disease, Huntington's disease, Amyotrophic Lateral Sclerosis, down's Syndrome, Korsakoff's disease, or epilepsy.

68. A method of any one of claims 42-67 wherein GDF-1 or a fragment or derivative thereof is administered to the mammal.

69. A method of claim 68 wherein the administered GDF-1 is encoded by SEQ ID NO:1.

70. A method of claim 68 wherein the administered GDF-1 or fragment or derivative thereof is encoded by a nucleic acid that comprises a sequence that has at least about 70% sequence identity to SEQ ID NO:1.

71. A method of claim 68 wherein the administered GDF-1 or fragment or derivative thereof is encoded by a nucleic acid that comprises a sequence that has at least about 80%, 90% or 95% sequence identity to SEQ ID NO:1.

72. A method of claim 68 wherein the administered GDF-1 or fragment or derivative thereof is encoded by a sequence that hybridizes to SEQ ID NO:1 under normal stringency conditions.

73. A method of claim 68 wherein the administered GDF-1 or fragment or derivative thereof is encoded by a sequence that hybridizes to SEQ ID NO:1 under high stringency conditions.

74. A method of claim 68 wherein the administered GDF-1 or fragment or derivative has at least about 70% sequence identity to SEQ ID NO:2.

75. A method of claim 68 wherein the administered GDF-1 or fragment or derivative has at least about 80%, 90% or 95% sequence identity to SEQ ID NO:2.

76. A method of claim 68 wherein the administered GDF-1 has the sequence shown in SEQ ID NO:2.

77. A method of any one of claims 42-67 wherein a nucleic acid encoding GDF-1 or a fragment or derivative thereof is administered to the mammal.

78. A method of claim 77 wherein the nucleic acid is SEQ ID NO:1, or the complement thereof.

79. A method of claim 77 wherein the nucleic acid has at least about 70, 80 or 90 percent homology to SEQ ID NO:1, or the complement thereof.

80. A method of anyone of claims 42-67 wherein NT-3 is administered.

